THE AMERICAN
JOURNAL OF PHARMACY

VOL. 107 NOVEMBER, 1935 NO. 11

EDITORIAL

THE CHEMICAL REVOLUTION

This is printed exactly as transmitted from the Auditorium of the Franklin Institute—whose series of such broadcasts "Scientific Wonders", under the direction of Major Coulson, are a welcome relief to much of the ether disturbance that the long waves carry to our ears.

MAJOR COULSON:
Necessity, the old adage tells us, is the mother of invention. If that is the case then economic depression, such as America and the world has been experiencing must be a stern and exacting step-mother, demanding ever quicker and more efficient performance from the youth entrusted to her not too tender care. But invention in America, and especially chemical invention, has no need to hang its head before its hard-featured, cold-eyed foster parent. Chemical invention has stepped out and shown what it could do when things were tough. Just what it has achieved is not generally known and what it may do in the future is even less known. That is my apology for selecting this subject for tonight's talk. We have an old friend and past master in the art of exposition to inform us.†

C.—There is much anxiety among the general public about the threatened exhaustion in natural fuels, Doctor, what is chemistry doing to remedy this?

Dr.—There indeed is much speculation concerning the depletion of our known storehouses of energy but it is largely due to the vaporings and mouthings of people who write for a living—who serve the froth for the beverage—and who are not the true interpreters of

† The Editor, exercising his prerogative, has omitted the paragraph which represented Major Coulson's gracious introduction of the speaker.

science. The whirling progress of the present, so alarmists state, is consuming its capital of resources. The world is being impoverished they say, and posterity embarrassed by the lavishness of the current generation, in its expenditure of coal and petroleum residues.

To the scientist, however, this gives but little concern. He knows that posterity will not be long embarrassed, for with the insight already gained into the energy changes of reacting chemicals, and the possibility of growing more motive fuel as we grow our body fuel—new sources of energy will be found long before our natural resources have been exhausted.

In England after Waterloo all good Englishmen planted acorns so that Britannia might ever rule the waves and never lack for sturdy oak wherewith to build her battleships. It was an idea consummated in pure loyalty, but it bespoke no real vision. For the Englishman today builds his battleship of bands of steel—and his oaks are only fashioned for his coffin.

Concern for the exhaustion of our fuel sources is just as unseemly and as irrational as the oak planting notion. Of course, conservation is wise and necessary, but there is no need for extravagant alarm in this direction. Our supply of petroleum will sometime run short, in a few decades, according to estimates by the U. S. Geological Survey, and neither the condensates from natural gas nor from lignite and coal will fill our power needs. Sooner or later, we must grow our fuel, as we grow our body fuel, from year to year.

C.—Do you mean we must grow it literally and actually like cabbages and potatoes?

Dr.—Precisely. It is interesting to recall a prophecy of Dr. Diesel shortly before his mysterious disappearance from the night boat that was carrying him from Germany to England. He foresaw the time when mineral oil would be exhausted and then, he said, supremacy of the seas would go to that power which possessed the most tropical territory for growing vegetable oil. Dr. Diesel has been dead but ten years, yet already on African coasts boats are run with palm, cottonseed, and peanut oils, and on the Continent automobiles are actually operated with rectified whiskey. Diesel engines are reported to run on less than ten ounces of cottonseed oil per British horsepower at a thermal efficiency of 24.5 per cent.

C.—Then growing our fuel is not so impractical as it sounds?

Dr.—Why, we grow a great deal of it as it is. Take the pro-

duction of alcohol for instance. A little active seed is planted. Out of the earth and out of the sun-flooded ether the little seedling draws its sustaining energy. Man cuts it down, soaks it in water for a while, and through the agency of an added yeast cell, changes its starch to sugar and thence to alcohol. The energy bound up by the plant is now contained in the alcohol, whence it can be promptly employed when needed. In alcohol there is great promise as a fuel, for the forces that the little seedling drew out of the earth and out of the sunlight are now locked in the atomic embrace of the fluid alcohol, only awaiting an opportunity to work. One has only to imbibe a portion of it to know its availability in this direction. And Europe is ahead of us in using alcohol as motor fuel.

C.—Is there anything further to be exploited in the way of power sources?

Dr.—A great deal. It is in the integral forces of the atom that man may someday find his greatest fund of energy. The physico-chemical studies of radium and radium emanations are still very incomplete, but we know that compressed into the atoms of this amazing element as well as its ninety odd elemental companions, is an immeasurable amount of electronic power. Some day, perhaps, this or solar energy and other similar forces will be harnessed in the service of man—whirling the buzzing wheels of industry—changing night into day—mounting the dizzy avenues of the air and coursing steadily through the lanes of ocean commerce.

C.—It sounds very much like magic, Doctor.

Dr.—Yes, it does, but chemistry, juggling its molecules is only an infant magician. Each year brings out a host of new products. There are boundless fields still unexplored, endless combinations still untouched. Agricultural industry owes chemistry a huge debt of gratitude. Time was when the world's supply of fixed nitrogen—that is fertilizing, nutritional nitrogen, so essential to the promotion of life, was rapidly dwindling away in spite of insanitary pelicans whose body wastes piled high had furnished the world with much of its nitrogen riches. Burning forests and big guns in action consumed much more of this very necessary nutritional nitrogen than the sun and germ and thunderstorm could replace. Then to make matters worse man turned to burning his brother, instead of burying him in the earth whence he came. Cremation was then a chemical crime, for it robbed the earth of much potential fertilizer. Had this process

of depletion continued for several hundred years with no replacement, the world would have been short of fixed nitrogen—a calamity little short of destruction. For a barren moonlike earth would fail to feed its human parasites. But along came the chemist again, and captured the unused free nitrogen of the air—changed it to fixed nitrogen and made the world evermore safe for hungry democracy. This discovery has notably increased the fertilizing of the soil and the conditions of rural industries are thus vastly bettered.

C.—The problem of food supplies is naturally one which creates great interest and it seems to me that chemistry has been working in this field by striving to find new sources of fertilizers. What is the situation there?

Dr.—That is the domain of biological chemistry. It has found and will continue to find other fertilizing agencies. It is nothing strange today to call to the farmer's help a willing, tireless army of little germs to prod his crop from the backward to the more forward stage. These little biological exhorters hang on to the grain rootlets, gather free nitrogen from the air, change it into assimilable, necessary compounds and feed it to the plants. Thus, the most barren soil can be made to support useful vegetable life.

Berthelot, the famous French chemist, once said: "The problem of food is a chemical problem. Whenever energy can be obtained economically we can begin to make all kinds of aliment, with carbon borrowed from carbonic acid, hydrogen taken from water, and oxygen and hydrogen taken from the air. The day will come when each person will carry for his nourishment his little nitrogenous tablet, his pat of fatty matter, his package of starch or sugar, his vial of aromatic spices suited to his personal taste; all manufactured economically and in unlimited quantities; all independent of irregular seasons, drought, and rain, of the heat that withers the plant and of the frost that blights the fruit; all free from pathogenic microbes, the origin of epidemics and the enemies of human life. On that day chemistry will have accomplished a world wide revolution that cannot now be estimated. There will no longer be hills covered with vineyards and fields filled with cattle. Man will gain in gentleness and morality because he will cease to live by the carnage and destruction of living creations. The earth will be covered with grass, flowers, and wood and in it the human race will dwell in the abundance and joy of the legendary golden age—provided that a spiritual chem-

istry has been discovered that changes the nature of man as profoundly as our chemistry transforms material nature."

C.—That is a noble conception. And what of chemistry in the service of medicine, Doctor?

Dr.—It was a chemist and not a physician that brought the great truth to medicine. This was Pasteur, the son of a humble tanner from Arbois, lifted by the buoyancy of clear genius into that rare realm of pure science, whose boundless domains few humans are privileged to know. Pasteur, the living contradiction of Pope's famous couplet:

> One science only will one genius fit,
> So vast is Art so narrow human wit.

That was not so with Pasteur, for his inspiration led him on from science to science, explaining the old and establishing the new; harnessing chemistry to agriculture and biology to industry. And he was a pioneer, a blazer of new trails. The roads which he chose were the hardest, but they led always to kingdoms that had the things which men sought and longed for, but could not find for themselves.

This was the man who discovered the biological basis of infection. After him followed the discovery of antiseptics used in combatting bacteria. Then came also the discovery of the anaesthetics; ether, chloroform, and latterly ethylene and vinyl compounds, all evolved in the chemical laboratory.

The last quarter of a century has flooded the world with medicinal chemicals derived from every conceivable place and thing. From the cellular spaces of roots and rhizomes, from fractions of crude coal distillate, from desiccated animal tissues, from the minerals in earth's bosom, from everywhere have come remedial agents in response to the chemist's call. And countless more await his beckoning.

And, no matter how the so-called interpreters of popular science may bring their message to the people, research in the sciences continues apace—every day marks progress.

Yet, today more than ever, Pasteur's prophetic-challenging call to the world must find a sane response.

"Take interest, I implore you, in those sacred dwellings which one designates by the expressive term: Laboratories. Demand that

they be multiplied, that they be adorned: these things are the temples of the future—temples of well-being and of happiness. There it is that humanity grows greater, stronger, better."

BABY OIL—For centuries it has been a custom to anoint very young babies with oil, in lieu of water washing. This all-over oiling procedure is usually followed for only a matter of a few weeks, but oiling following a soap-and-water washing may continue for a long time. Finally, a little oil is applied locally just to inflamed areas. Normally, the oil used has been the ever present olive oil of southern Europe, for which cottonseed oil and corn oil became widely substituted in this country. Recently there has appeared a strong trend toward specially prepared oils for this purpose, with properties other than mere oiliness.

The modern baby oil, besides being blended from several kinds of oils, to secure the right spreading and coating properties, contains preservatives which keep it from becoming rancid and hence irritating, and, what is more important, is made antiseptic toward the types of bacteria found on the skin. In addition, it is pleasantly perfumed, so that the rite of application is attended by an aura of impressive fragrance.

The earlier attempts at surface antisepsis were made by rubbing mercury compounds on the skin, with or without oiling, a drastic procedure not entirely free from chance of irritation and of poisoning, and only partially effective at best in preventing or curing skin diseases. Antiseptic oils avoid the use of mercury, using instead the newer synthetic germicides. The effectiveness of antiseptic oil has been so demonstrable that it has been adopted by a number of the better maternity and babies' hospitals. Indeed, some superintendents have become so enthusiastic over its record in the prevention of impetigo and other highly contagious skin diseases that they have made its use a feature of their treatment and recommended it for continuation in the home, often up to the age of six months or more.

Several manufacturers have watched with wonder and chagrin as the market for packaged talcum powder has shrunk with rapidity, while baby oil has become an article of commerce with its volume already reaching sizeable proportions.—(*Little Ind. Bulletin*).

ORIGINAL ARTICLES

THE MICROSCOPY OF POWDERED DESICCATED ENDOCRINE GLANDS*

By Heber W. Youngken, Ph. D., Sc. D.

THE steady increase in the employment of powdered desiccated endocrine glands within recent years in the treatment of disease owing to a deficiency in or an unbalanced condition of the internal secretions has resulted in a greatly enhanced production of these products and the consequent need of biological and microscopical methods of valuation for them.

It has become obvious that biological assays alone would not entirely satisfy the purity nor the identity standards of these materials and that without microscopic descriptions of them they would be prone to adulteration with undesirable organic cellular materials by unscrupulous persons.

The literature had been searched and no available records of microscopical standards for these products could be found.

In the December, 1933, number of the *Journal of the American Pharmaceutical Association* (1) the author published the results of some preliminary studies made upon the microscopy of a number of these glandular products. Since that time the investigation has been continued and extended to include additional products, the main results of which are herewith reported. The glandular materials studied were obtained from cattle and hogs, and, in the cases of thyroid and pituitary, also from sheep.

Powdered Desiccated Thyroid

Description and physical properties—A yellowish to buff-colored amorphous powder having a slight characteristic, meat-like odor and a saline taste.

Histological characteristics—When suitably mounted and examined under the microscope, thyroid shows numerous smooth to striated hyaline fragments of colloid, of angular to irregular shape, which are colorless to pale yellow in water mounts, brown in Mallory's

*Presented to Sect. N_3, A. A. A. S., Minneapolis meeting, 1935.

stain and pink in eosin solution, some of these fragments containing granules, minute vacuoles, crystalloidal bodies and cells; numerous irregular fragments of follicular epithelium staining brown with Mallory's stain, the individual cells more or less polygonal to rounded-angular or irregularly cuboidal, often with prominent nuclei staining dark blue, their cytoplasm purplish with Delafield's hematoxylin; slender glistening segments of neuraxons; numerous aggregates of particles of intercellular substance and slender, mostly straight, connective tissue fibers staining blue to greenish blue with a mixture of Mallory's stain and 1 per cent. phosphotungstic acid; the bundles of fibers often appearing reddish in plain Mallory's stain; few glistening fragments of blood vessels with serrated or crenated ends as viewed in water mounts. Both the colloid and the follicular epithelium are also colored brown by a mixture of equal parts of Mallory's stain and 1 per cent. phosphotungstic acid solution.

Powdered Desiccated Suprarenal

Description and physical properties—A light yellow to brown amorphous powder having a slight characteristic odor. No disagreeable odor suggestive of putrefaction is present.

Suprarenal is only partially soluble in water.

Histological characters—Numerous chromophil (chromaffin) cells, both isolated and in loose aggregates, the individual cells stellate to irregular with spheroidal to oval nuclei and granular cytoplasm which take a brownish coloration with chromic acid T. S.; numerous clear, jointed segments of non-medullated nerve fibers, the axons of which are colored mauve with eosin and hematoxylin T. S.; numerous cortical cells both isolated and in masses, the individual cells cuboidal to irregularly rounded with spheroidal nuclei, some of the cells containing tiny fat globules, granules or pigment, the chromatin of the nucleus and granules staining blue and the protoplasm red to purple with Delafield's hematoxylin T. S. and alcoholic eosin; numerous fragments of connective tissue fibers, fibrocytes and intercellular substance, the fibers wavy, the fibrocytes slender, linear to fusiform, and all colored blue with a mixture of Mallory's stain and phosphotungstic acid T. S.; numerous minute granules of crystalline appearance and irregular form and many isolated nuclei; few elastic fibers.

Powdered Desiccated Whole Pituitary

This occurred as a gray to yellowish gray amorphous powder with a characteristic odor and a saline and disagreeable taste.

The microscopical elements detected were as follows:

Numerous yellowish masses of polyhedral cells surrounded in parts by connective tissue, the latter staining blue with a mixture of Mallory's stain and 1 per cent. phosphotungstic acid solution; numerous large, polyhedral chromophile cells with central rounded nuclei and coarse cytoplasmic granules staining red with acid fuchsin, the nuclei colored blue and the cytoplasm reddish purple with eosin and methylene blue solution; numerous altered, cubical to low columnar chromophobe cells with or without distinct cytoplasmic granules whose nuclei are stained light blue and cytoplasm paler blue with eosin and methylene blue, both chromophile and chromophobe cells frequently with minute fat droplets colored brown to black with 0.5 per cent. osmic acid solution; few cells containing a colloidal substance and appearing pale greenish to greenish yellow in water mounts; few segments of blood vessels of tubular, hyaline nature, the cut ends of which showed serrated dark outlines when examined in silver nitrate solution; numerous mossy neuroglia fragments, the cells with spherical nuclei and elongated, branching processes when viewed in phosphotungstic acid and hematoxylin reagent, a few small faintly basophilic, polyhedral cells from the pars intermedia with pale blue nuclei and a pink, granular cytoplasm when stained with hematoxylin and eosin; a number of angular hyaline fragments; fragments of nerve fibers with or without a bulbous end, the axons of which are colored mauve with eosin and hematoxylin; a few cells colored black with osmic acid solution; a number of spindle-shaped, bipolar nerve cells.

Powdered Desiccated Anterior Pituitary

This occurs as a yellowish brown amorphous powder with a characteristic odor and saline taste. It is partially soluble in alcohol, ether, water and acetone.

The histological elements detected were as follows:

Numerous yellowish masses of polyhedral cells surrounded in parts by connective tissue, the latter staining blue with Mallory's stain; numerous large polyhedral chromophile cells with central

rounded nuclei and coarse cytoplasmic granules staining red with acid fuchsin, the nuclei colored blue and the cytoplasm red-purple with eosin and methylene blue solution; numerous cubical to low columnar chromophobe cells with or without distinct cytoplasmic granules whose nuclei are stained light blue and cytoplasm paler blue with eosin and methylene blue, both chromophile and chromophobe cells frequently with fat droplets colored brown to black with 0.5 per cent. osmic acid solution; colloidal material occurring between certain of these cells appearing greenish in water mounts; a few scattered cylindrical nerve fibers often attached to fragments of blood vessels, appearing hyaline in water mounts, their axis cylinders staining a mauve color with eosin and hematoxylin solution; few segments of blood vessels with cut ends showing crenate inner endothelial margins and best seen in silver nitrate solution; a few spheroidal cells with reddish brown lipoid content colored black with 0.5 per cent. osmic acid solution; a few fragments of colloidal substance of greenish aspect in water mounts.

Powdered Desiccated Posterior Pituitary

This occurs as a yellowish or grayish amorphous powder with a characteristic odor and a saline, disagreeable taste. It is partially soluble in water, alcohol, ether and chloroform.

The following histological elements were detected:

Numerous fragments of neuroglia tissue (mossy neuroglia) with spheroidal nuclei and long, slender, branching processes best distinguished with 1 per cent. phosphotungstic acid and hematoxylin which stains the nuclei blue and the processes bluish black; numerous spindle-shaped bipolar nerve cells; a number of ovoid, multipolar nerve cells whose cell bodies sometimes contain pigment granules and whose several processes appear bluish black in phosphotungstic acid and hematoxylin mounts; fragments of nerve fibers with or without a bulbous end, some of the bulbous ends of which are surrounded by cells containing a greenish yellow colloidal substance; the axons of the nerve fibers colored mauve with eosin and hematoxylin solution; a few amyloid bodies of ovoid or crescent shape staining a deep purple with iodine water; many irregular hyaline fragments.

Powdered Desiccated Whole Ovary

This product occurs as a pale buff to yellowish brown, amorphous powder, the predominance of yellow or brown in the color combina-

tion depending upon the ratio of corpus luteum to other ovarian substance, the species of the animal yielding the product and the period at which the ovaries were removed from the animal. It possesses an odor resembling ground mash and a salty, disagreeable taste. It is slightly soluble in water, alcohol, ether and petrolic ether.

The following histological elements were observed:

Numerous young, unicellular follicles and fragments of older Graafian follicles, the young follicles appearing as spherical to oval-shaped bodies containing a central cell or oocyte which is colored deep blue with Heidenhain's hematoxylin and alum solution; surrounding the oocyte in older follicles occurs a single layer of flattened follicular cells resembling the germinal epithelial cells whose nuclei are stained deep blue with Delafield's or Heidenhain's hematoxylin, while attached to parts of the follicle is a small amount of connective tissue which is colored pink with eosin solution and blue with a mixture of Mallory's stain and 1 per cent. phosphotungstic acid test solution; a few more or less distorted cubical to low columnar and transitional germinal epithelial cells occurring singly or in groups with a round central nucleus and granular cytoplasm, the granules glistening in water mounts, the nucleus staining a deep blue with Delafield's hematoxylin; a number of small, compact masses of dense, white fibrous connective tissue consisting of white collagenous fibers and fibrocytes, the fibers appearing long, narrow, transparent, with distinct pointed ends, difficult to discern in water mounts, but swelling and visible in a mixture of 1 per cent. acetic acid and ss. picric acid, and staining a brilliant red in acid fuchsin, the bundles of fibers showing numerous fibrillæ which exhibit a dark outline when mounted in 3 per cent. aqueous solution of silver nitrate, the fibrocytes appearing irregularly polygonal to slightly elongated, usually forked at one end in surface view and spindle-shaped in profile view, the nuclei staining a deep blue and the cytoplasm a pale blue to purplish blue with Delafield's hematoxylin; few scattered spindle-shaped, smooth muscle fibers with centrally placed nucleus clearly visible in gold chloride T. S.; few capillaries of tubular, hyaline nature, occasionally branched and grayish to grayish black in outline with 1 per cent. silver nitrate solution; fragments of larger blood vessels with circular to oval cut ends, their endothelial layer spherical cells containing globules of lipoid substance which stains black with 1 per cent. osmic acid solution; scattered segments of non-medullated

nerve fibers of cylindrical form and consisting of neuraxon and neurolemma, the neuraxon taking a blue color with Delafield's hematoxylin, a mauve color with hematoxylin and eosin solution and a deep red with acid fuchsin; numerous interstitial cells of rounded to ovate form, some of them slightly beaked, containing granules and shining fat globules, their nuclei staining a deep blue and their cytoplasm a pink color with hematoxylin and eosin; numerous lutein cells appearing yellow in water mounts; when the material contains corpora lutea, the cells large, polyhedral to oval, often in masses, each containing a central nucleus, lutein granules and fat droplets.

Powdered Desiccated Ovarian Residue

This represents the whole ovary from which the corpus luteum has been separated by means of a scalpel, ground, dried, powdered and sifted. But the perfect separation of corpus luteum is not always carried out in practice.

The powder, therefore, contains the same elements as that of powdered, desiccated whole ovary but only a relatively small number of lutein cells.

It may also be distinguished from powdered, desiccated whole ovary by the following test:

When 1 gm. of ovarian residue is mixed with 1 cc. of sulphuric acid, a yellowish green or fig color is produced.

Upon the addition of about 0.5 cc. of old ammonium polysulphide to this mixture, a yellow color is produced which immediately changes to white.

Powdered Desiccated Corpus Luteum

A yellow to buff-colored amorphous powder with a characteristic, malt-like odor and a saline taste. It is partly soluble in water, alcohol, petrolic ether and ether. The color varies with the stage of pregnancy of the animal and with its age.

The histological features of this product are as follows:

Numerous hypertrophied, yellowish lutein cells occurring singly or in small groups or irregular masses, the lutein cells polyhedral, ovoid, oblong to irregularly elongated with a rounded, central nucleus staining deep blue and cytoplasm staining purple with Delafield's hematoxylin, many of these cells containing fat globules and lutein

granules which take a black color with 0.5 per cent. osmic acid, the lutein cells and granules staining greenish to greenish blue in 10 per cent. sulphuric acid; between various lutein cells in a clump occur connective tissue septa which are colored deep red with acid fuchsin and bluish with a mixture of Mallory's stain and 1 per cent. phosphotungstic acid; occasional capillaries of cylindrical shape, sometimes branched, hyaline, and showing black outlines in 1 per cent. silver nitrate solution; occasional fragments of large blood vessels whose severed ends exhibit a serrate or crenate endothelium; very few non-medullated nerve fibers, the axon-colored mauve with eosin and hematoxylin, the fibrillæ clearly seen in a mixture of phosphotungstic acid and Mallory's stain; a few spindle-shaped, smooth muscle fibers with central nucleus colored deep blue with hematoxylin; a number of amyloid bodies colored purple to violet with iodine water; a faint yellow, colorless crystalline substance.

Summary and Conclusions

1. The more important results of studies made by the author upon the microscopy of powdered desiccated endocrine glands obtained from cattle and hogs and, in the case of thyroid and pituitary from sheep also, are presented with a view toward providing microscopical standards for these biological products which are becoming more and more extensively employed in modern organotherapy.

2. Descriptive microscopical standards are presented for powdered desiccated thyroid, suprarenal, whole pituitary, anterior pituitary, posterior pituitary, ovary, ovarian residue, and corpus luteum.

3. Powdered desiccated thyroid may be identified by its smooth to striated, hyaline fragments of colloid, some of which contain granules, minute vacuoles, crystalloidal bodies and cells together with the numerous, irregular fragments of follicular epithelium, both of which stain brown with a mixture of Mallory's stain and 1 per cent. solution of phosphotungstic acid.

4. Powdered desiccated suprarenal may be identified by its numerous, characteristically stellate to irregularly shaped chromophil (chromaffin) cells which take a brown coloration with chromic acid test solution together with its characteristic cortical cells as examined in Delafield's hematoxylin and alcoholic eosin.

5. Powdered desiccated whole pituitary may be identified by the numerous large, polyhedral or chromophile cells which possess coarse granules and show a distinct affinity for acid stains, acid fuchsin coloring them red, the presence of many chromophobe cells of more or less cubical, rounded or pyriform shape with few or no fine granules whose nuclei are colored blue and cytoplasm a paler blue with either Delafield's hematoxylin or a mixture of eosin and methylene blue solution, the mossy neuroglia cells clearly visible in a mixture of 1 per cent. phosphotungstic acid and Delafield's hematoxylin and by the presence of bipolar nerve cells.

6. Powdered desiccated anterior pituitary can be identified by the presence of characteristic chromophile and chromophobe cells and the absence of mossy neuroglia and bipolar nerve cells.

7. Powdered desiccated whole posterior pituitary can be identified by the presence of characteristic numerous mossy neuroglia cells and bipolar and multipolar cells and the absence of chromophile and chromophobe cells.

8. Powdered desiccated whole ovary or "ovarian substance" may be identified by the presence of more or less distorted cubical to low columnar epithelial cells whose nucleus takes a deep blue and cytoplasm a pale purple to pink color with Delafield's hematoxylin, by the rounded to irregular masses consisting of primary oocytes surrounded by connective tissue elements, the rounded to oval interstitial cells containing granules and fat droplets staining bright red with red acid dyes, the numerous fibroblasts with forked ends, the numerous lutein cells, often in masses, which appear yellowish in water mounts together with an abundance of dense connective tissue consisting mostly of narrow collagen fibers which swell and are colored yellow in a mixture of 1 per cent. picric acid and 1 per cent. acetic acid solution.

9. Powdered desiccated ovarian residue shows a similar microscopic picture to powdered desiccated whole ovary except for the almost complete absence of corpus luteum material.

10. Powdered desiccated corpus luteum is characterized by its numerous lutein cells, isolated or in masses, the individual cells somewhat polyhedral with spheroidal central nucleus and numerous lutein granules and fat droplets, the groups of lutein cells inter-

mingled with fine collagen fibers and appearing yellowish or greenish-yellow in water mounts.

The author desires to gratefully acknowledge the kindness of The Wilson Laboratories, Armour & Co., Parke, Davis & Co. and Burroughs Wellcome and Co., who contributed glands and glandular products used in this research.

Massachusetts College of Pharmacy, Boston, Mass.

June 14, 1935.

REFERENCE

1. Youngken, H. W., and Reed, A. W.: A New Field of Investigation in Pharmacognosy: The Microscopy of Glandular Products. *Jour. A. Pharm. Assoc.* **22**, 1215-1218 (1933).

HONEY, AN ANCIENT DRESSING FOR WOUNDS—Honey as a dressing for wounds was popular at one time in the Middle Ages. Still earlier, during the Roman Empire, it enjoyed a certain vogue; and Pliny refers in a certain passage to fish fat and honey as making a good ointment for wounds. It may well be that the fish fat he refers to was cod liver oil.

Now honey has been rediscovered as a remarkably effective ointment. In a Red Cross hospital in Hamburg, Germany, tests have been carried out with honey during the past half year, and it has been found that even contaminated wounds quickly become cleaner under its influence. But though it cleans a wound, it does not seem to make it heal more quickly than before. As cod liver oil promotes rapid healing, it has been combined with honey in an ointment so as to achieve the double purpose of cleansing and healing.

So in this respect we are back again in the days of Pliny, after many a digression and much circumspection.

How does honey act? Does it cause beneficial fermentation? And which of its many component parts is most potent; its sugar, mineral salts, plant acids, higher alcohols or some ferment? Doubtless the Germans, with their methodical instincts, will isolate each of the component elements of honey, and will try each in turn on a number of cases of varicose ulcers, wounds, etc. Pending conclusive findings from these future experiments, tests with whole honey will be continued.—(*Science News Letter*).

FURTHER STUDY OF DERIVATIVES OF DIPHENYL ETHER*

By L. Chas. Raiford and John C. Zimmerman

THIS work was done to extend previous observations on the derivatives of diphenyl ether (1) and in particular to identify a compound obtained by Raiford, Thiessen and Wernert (2) when one of these products was nitrated.

In the previous work it was found that nitration of 4-nitro-4′-bromodiphenyl ether displaced the halogen and gave Willgerodt's (3) 2,4,2′,4′-tetranitro derivative. When the 4-nitro-2′,4′-dibromo ether was nitrated the chief product (4) was a trinitro compound that contained all the bromine of the starting material and was shown not to be an impure sample of the isomeric 2,4,6-trinitro-2′,4′-dibromodiphenyl ether, m. p. 163-164 degrees, which was synthesized for this comparison from picryl chloride and 2,4-dibromophenol. It is now found that treatment of the product in question with piperidine as directed by LeFevre and others (5) causes scission and gives 2,4-dinitrophenylpiperidine (6) and 2,4-dibromo-5-nitrophenol (7). This shows that the ether under consideration is 2,4,5′-trinitro-2′,4′-dibromodiphenyl ether.

Occasion was also taken to test further the action of piperidine on the substituted diphenyl ethers indicated below. The first two from Table I were readily split and 2,4-dinitrophenylpiperidine and the required phenols were isolated and identified. The third one gave tar and indefinite results. From Table II ethers 2, 4 and 6 were tested. In each case scission occurred and the required phenol was isolated and identified. The other product was not the expected 2,4,6-tripiperidino-1,3-dinitrobenzene. It is still under consideration.

Experimental Part

These ethers were prepared from 2,4-dinitrochlorobenzene and 2,4,6-tribromo-1,3-dinitrobenzene respectively. The latter was obtained by nitration of sym-tribromobenzene with fuming nitric acid by Jackson and Koch's (8) method modified to the extent that the mixture was warmed in a flask connected by a ground glass joint to a

*Contribution from the Laboratory of Organic Chemistry of the State University of Iowa.

reflux condenser until solution took place and then allowed to stand at room temperature until crystallization was complete. To obtain the ethers these nitro compounds were treated with the required alkali phenolates, as already described (9), modified to meet the requirements of individual cases. Analytical data are given in tabular form on pages 474-475.

Summary

1. The structure of the product previously obtained by nitration of 4-nitro-4'-bromodiphenyl ether has been established by scission of the compound with piperidine.

2. When other ethers of this class, having more complex structures and containing larger numbers of substituents, were tested with piperidine, scission took place, but the required phenols only have thus far been identified.

3. Further work in progress.

BIBLIOGRAPHY

(1) Raiford and Colbert: *J. Am. Chem. Soc.*, **48**, 2652 (1926).

(2) Raiford, Thiessen and Wernert: *J. Am. Chem. Soc.*, **52**, 1205 (1930).

(3) Willgerodt: *Ber.*, **13**, 887 (1880).

(4) In a number of repetitions of this experiment, though not in all, a small amount of Willgerodt's compound was also isolated.

(5) LeFevre, Saunders and Turner: *J. Chem. Soc.*, 1168 (1927); 512 (1929).

(6) Lellman and Geller: *Ber.*, **21**, 2283 (1888).

(7) Garzino: *Atti R. Accad. Sci. Torino*, **25**, 275 (1869).

(8) Jackson and Koch: *Am. Chem. J.*, **21**, 519 (1899).

(9) Ref. 2, 1207.

TABLE I

ARYL ETHERS OBTAINED FROM 2,4-DINITROCHLOROBENZENE

Substituent introduced into position 1	Crystal form	M. P. °C.	Formula	Analyses			
				Nitrogen, %		Halogen, %	
				Calc'd	Found	Calc'd	Found
4-Oxydiphenyl-	Yellow plates [a]	115	$C_{18}H_{12}O_5N_2$	8.33	8.31	...	...
3-Bromo-4-oxydiphenyl-	Amber plates [a]	203–204	$C_{18}H_{11}O_5N_2Br$	...	...	19.27	19.45
3,5-Dibromo-4-oxydiphenyl-	[b]	328–333 decomp.	$C_{18}H_{10}O_5N_2Br_2$	...	...	32.38	33.86

a. Crystallized from acetic acid.

b. The residue left after extraction with hot acetic acid was dissolved as far as possible in chloroform, and from this solution the product was precipitated by the slow addition of ligroin.

TABLE II

TABLE II

ARYL ETHERS OBTAINED FROM 2,4,6-TRIBROMO-1,3-DINITROBENZENE

Radicals introduced into positions 2,4,6	Crystal form [a]	M. P. °C.	Formula	Analyses			
				Nitrogen, %		Halogen, %	
				Calc'd	Found	Calc'd	Found
Phenoxy-	Needles [b]	99	$C_{24}H_{16}O_7N_2$	6.30	6.51	...	...
4-Chlorophenoxy-	Yellow needles	157	$C_{24}H_{13}O_7N_2Cl_3$	...	...	19.45	19.30
2,4-Dichloro-	Plates	184	$C_{24}H_{10}O_7N_2Cl_6$	...	...	32.71	32.78
2,4,6-Trichloro-	Yellow needles	169	$C_{24}H_7O_7N_2Cl_9$	...	...	42.34	42.39
2-Bromo-	Brown needles	213	$C_{24}H_{13}O_7N_2Br_3$	...	...	35.24	35.11
4-Bromo-	Plates [b]	142	$C_{24}H_{13}O_7N_2Br_3$	...	...	35.24	35.08
2,4-Dibromo-	[c]	230–232	$C_{24}H_{10}O_7N_2Br_6$	...	...	52.45	52.01
2,4,6-Tribromo-	[d]	245–247	$C_{24}H_7O_7N_2Br_9$	...	...	62.33	62.48
4-Nitro-	Brown needles	271–272	$C_{24}H_{13}O_{13}N_5$	12.09	12.29	...	...
2-Nitro-4-chloro-	Yellow plates [e]	208–209	$C_{24}H_{10}O_{13}N_5Cl_3$	...	...	15.60	15.51
2-Nitro-4-bromo-	Brown	152–153	$C_{24}H_{10}O_{13}N_5Br_3$	...	...	29.41	29.17
4-Oxydiphenyl-	Plates [b]	159	$C_{42}H_{28}O_7N_2$	4.16	3.89	...	...
3,5,4′-Tribromo-4-oxydiphenyl-	[f]	293–295 decomp.	$C_{42}H_{19}O_7N_2Br_9$	...	...	52.06	51.39

a. Reaction products were usually mixed with some starting material which was removed by extraction with alcohol—acetic acid (2:1), after which the residue was crystallized from glacial acetic acid. Yields could not be determined satisfactorily. No entry indicates amorphous material.

b. Crystals became dark colored in direct sunlight.

c. Residue left after removal of starting material was dissolved in benzene and treatment of this solution with ligroin precipitated amorphous solid.

d. Residue left after removal of starting material was dissolved in pyridine, and treatment of this solution with ligroin precipitated amorphous solid.

e. Unchanged 2-nitro-4-chlorophenol was removed by steam distillation.

f. Treatment of a chloroform solution of the product with ligroin precipitated an amorphous solid.

STATE REQUIREMENTS FOR ENTRANCE TO EXAMINATION FOR REGISTERED PHARMACIST

COMPILED BY NATIONAL ASSOCIATION BOARDS OF PHARMACY, CHICAGO. OCTOBER, 1935

State	High School Graduation	Pharmacy College Graduation	Experience with 4 yr. course	Exemptions from college and other information
Alabama	1/1/27	1/1/27	One year	Exemptions expired 7/1/32
Alaska	2 years	None		Five years experience
Arizona	2 years	6/20/35	One year	Assistants and others employed prior to 6/20/35 who registered for exemption prior to 9/18/35 and pass examination before 6/20/40 exempt from college; must prove up four years experience
Arkansas	1/1/25	7/1/30	One year	
California	1/1/28	1/1/28		Three-year course still recognized; college graduates must have four years experience (credit for college attendance time)—one year as assistant. Exemption from college for assists. registered prior to 1/1/34 who file five years experience, at least 2 yrs. under asst. license
Colorado	5/26/29	5/26/29	One year	Exemptions expired 5/26/34
Connecticut	1/1/23	1/1/25	One year	
Delaware	3/30/27	3/30/27	Two years	Those residing in Delaware five years prior to examination are exempt from college; must prove four years of experience, two years of which must be as asst. pharmacist
District of Columbia	3/4/28	3/4/28	One year	

State	High School Graduation	Pharmacy College Graduation	Experience with 4 yr. course	Exemptions from college and other information
Florida	6/1/28	6/1/28	One year	Exemption from college for those with 1 yr. experience under R. Ph. prior to June, 1925
Georgia	8/1/27	1/1/34	One year	Experience prior to 3/8/33 exempts from college for three years
Idaho	5/1/25	5/1/25	One year	Exemptions expired 5/1/30
Illinois	1/1/20	7/1/17	Two years	Apprentices prior to 7/1/17 exempted from college
Indiana	7/1/23	1/1/20	One year	Exemption for apprentices and assistants prior to 1/1/20; special exemption for assistants on roster at time of passage in 1935, but must pass exam. before October, 1936.
Iowa	7/1/25	7/1/17-2 yr 7/4/36-grad	One year	Exemptions expired 7/1/24. Until 7/4/36, two years college and two years experience
Kansas	5/25/21	5/28/29	One year	Exemptions applying only to Kansas residents expired June, 1934
Kentucky	1/1/26	7/1/24	Two years	
Louisiana	1/1/28	1/1/28	One year	Exemptions expired 1934
Maine	7/1/27	6/19/31	One year	Those employed six mos. prior to 6/19/31 exempt from college until 6/19/36
Maryland	6/1/20	6/1/20	One year	
Massachusetts	None	None		Four years of experience; credit for actual time in college in lieu of experience

State	High School Graduation	Pharmacy College Graduation	Experience with 4 yr. course	Exemptions from college and other information
Michigan	1/1/24	1/1/29-2 yr 1/1/38-grad	One year	Two years experience with two years college until 1938
Minnesota	1/1/20	4/23/19-2 yr 3/28/29-grad	One year	Assistants or those with experience prior to 4/23/19 exempt from college if proper affidavits were filed 3/28/30
Mississippi	1/1/21	1/1/21	None	
Missouri	1/1/23	Jun '34-1 yr Jun '35-2 yrs Jun '36-3 yrs Jun '37-4 yrs		Four years experience with credit for actual time of attendance at college
Montana	1/1/26	1/1/26	One year	Exemptions expired April, 1935. Four-year course compulsory 1/1/26
Nebraska	7/1/20	1/1/30-1 yr	Six mos	1 yr. college—3 yrs. experience; 2 yrs. college—2 yrs. experience; 3 yrs. college—1 yr. experience; 4 yrs. college—6 mos. experience
Nevada	1/1/14	None	One year	Five years experience
New Hampshire	1/1/27	1/1/39	Two years	Four years experience for non-graduates until 1939
New Jersey	9/1/23	9/1/20	see next column	After 7/1/36, four years experience in approved pharmacy, with maximum credit of three years for college attendance time. One full year of experience must be subsequent to graduation from college

State	High School Graduation	Pharmacy College Graduation	Experience with 4 yr. course	Exemptions from college and other information
New Mexico	1 year	5/20/35	One year	Exemption from college for those engaged in practice six months prior to 5/20/35 (enactment) who register for such exemption within one year and who file four years experience before 5/20/40
New York	1/1/25	1/1/04	Two years	Three-year college course still recognized
North Carolina	1/1/22	1/1/18-1 yr 1/1/22-grad	One year	
North Dakota	1/1/13	1/1/15	One year	
Ohio	1/1/20	8/26/15	None, if registered in pharmacy school for full 4 yrs	Four full years of apprenticeship prior to 7/1/17 exempts from college
Oklahoma	7/16/21	7/16/21-1 yr 7/15/23-grad	Two years	Exemption for assistants registered prior to 1/1/22
Oregon	1/1/18	7/1/22-2 yr 7/1/25-grad	One year	Four-year course compulsory 1928-1929
Pennsylvania	6/1/25	1/1/06	One year	Former 2 yr. grad.—4 yrs. experience; 3 yr. grad.—2 yrs. experience
Puerto Rico	3/12/27	3/12/27	None	
Rhode Island	1/10/10	1/10/10	None	
South Carolina	1/1/23	1/1/33	One year	

State	High School Graduation	Pharmacy College Graduation	Experience with 4 yr. course	Exemptions from college and other information
South Dakota	1/1/27	7/1/31	One year	Exemptions expired 7/1/33
Tennessee	4/17/19	None		Four years experience. Credit for actual college time not to exceed two years
Texas	1/1/26	6/12/34	One year	Exemptions expired 1934
Utah	7/1/25	7/1/27	One year	Four year college course compulsory 7/1/27
Vermont	1/1/29	None		Three years experience
Virginia	4/1/22	4/1/22	None	
Washington	7/1/14	7/1/14	None	Proof of 15 years experience prior to 6/8/27 exempts from college
West Virginia	1/1/23	1/1/23	Two years	
Wisconsin	1/1/26	7/28/27	One year	Assistants filing proof of employment at least one year immediately prior to 8/1/27 are eligible without college until 1/1/36
Wyoming	1/1/25	2/24/33	One year	Experience six months prior to enactment exempts from college until 7/1/36

Explanatory Notes

The dates given in the high school and college graduation columns indicate the initial date when such requirement went into effect.

The four-year college course in pharmacy became generally effective, by agreement of the American Association Colleges of Pharmacy and the National Association Boards of Pharmacy, for matriculation in 1932 (graduation 1936). Therefore, so far as the board examination is concerned, the date when the four-year course becomes compulsory is 1936. A few states, as indicated, made the four-year course obligatory to 1936.

All the states with the exception of California and New York have reciprocity agreements through the National Association Boards of Pharmacy. The general basis for reciprocity provides that an applicant is eligible by reciprocity in those states which would have admitted him to examination on the date of his original license, with the qualifications he possessed at that time. A careful checking of the chart will reveal the fact that the majority of the states now require graduation from the four-year course plus a minimum of one year of full time retail experience, under supervision of an R. Ph. If he has more retail experience than the one year minimum, he will also be eligible in the states that require more than one year of such time.

The experience requirements are shown in the two-right-hand columns. An attempt has been made to show the exact amount of experience required with the four-year course, to avoid the necessity for making interpretations from rules. In the few states where an applicant can still qualify without college training, the experience requirement is outlined in the extreme right-hand column.

H. C. Christensen, *Secretary N. A. B. P.*

Approximate Chemical Analysis of a Man (Moss). Height, 5 feet 8 inches; weight, 148 pounds. Quoted from *Practical Dietetics* by W. Gilman Thompson, M.D., Professor of Medicine in the Cornell University Medical College, New York.

Oxygen	92.4	pounds
Hydrogen	14.6	"
Carbon	31.6	"
Nitrogen	4.6	"
Phosphorus	1.4	"
Calcium	2.8	"
Sulphur	0.24	"
Chlorine	0.12	"
Sodium	0.12	"
Iron	0.02	"
Potassium	0.34	"
Magnesium	0.04	"
Fluorine	0.02	"
Total	148.00	pounds

All these elements are necessarily derived from food and water plus the oxygen of the air which is breathed.

THE APOTHECARY, A LITERARY STUDY

By Edward Kremers

No. 42. A Medico-Pharmaceutical Practitioner on "Six Frontiers"

"JOHN MARSH, PIONEER," * is, in a way, a medical companion to the pharmaceutical biography "A Quaker Forty-niner." In place of the New Jersey Quaker lad, who served his pharmaceutical apprenticeship in Philadelphia from 1832 until he had reached the age of twenty-one, we have the Puritan pupil of Andover and student of Harvard originally destined for the ministry but switching off to medicine. His ambition to become a full-fledged M. D. he does not realize. He reads medicine as opportunity offers with Dr. John Dixwell of Boston. Upon graduation from Harvard, he, in 1823, accepts a family tutorship at Fort Snelling in the hope to save enough money to return to his medical studies. The "trail-blazer on six frontiers" touches Detroit, Green Bay, "where he could have believed he was in France," and Prairie du Chien on his way to where now St. Paul and Minneapolis stand. At this army post he falls in with the post surgeon, Dr. Edward Purcell (photo opposite page 82), but fails to receive a statement certifying that he has "read medicine." With the transference of Col. Snelling, he loses his position as family tutor, but he does not return to New England. Not only had he acquired a taste for frontier life, he had held a temporary position as assistant to the Indian agent. This prepared him for a similar post at Prairie du Chien. At first eager to save money for his contemplated medical education, he becomes greedy for gold and sells fire arms to the Indians in violation of the law. Black Hawk's war and its precursor have made this a serious offense of which his enemies take advantage. He flees, first to New Salem, Illinois, where he leaves his motherless child, then to St. Louis, and finally via the Santa Fe trail to California.

His mate being half Canadian French, half Sioux, he is brought into close touch with the Indians, whom he assists with his medical knowledge and such drugs as he has at his disposal. On the way to California, he saves his own life by relieving an old Indian chief. In California, he again makes use of his medical knowledge and skill, not only to help the Indians but the early settlers as well.

*By Geo. D. Lyman, Chas. Scribner's Sons, 1930.

Unlike the Quaker Forty-niner, he did not come to California as a result of the gold rush, but much earlier, viz., in 1836. Not only is he the first American practitioner in this Mexican province, but he is one of the chief conspirators who turn the tide to union with the United States.

As a man, he is not the noble character among ignoble surroundings as his Quaker contemporary. In spite of his Puritan ancestry and bringing up, he not only falls away from Puritanic precepts so far as his mating with a half breed is concerned, but he does not have the courage to let his folks "down East" know what sort of life he lives. When asked whether a report that he is married be true, he denies it. This was true, legally, but not true ethically. As already pointed out, his greed led to legal troubles which caused him to leave Prairie du Chien. In California he becomes not only a hoarder of gold, but takes from a messenger boy his only fifty cents for some grapes promised him upon the delivery of a message. His Indians are his slaves, and he does not hesitate to demand half of the fortune (in cattle) of a settler for medical attendance upon his wife. True, on the other hand, he never hesitated to undertake long and dangerous trips on horseback, both in the Old Northwest frontier and in the extreme West, when called. Yet such is his closefistedness that he is hated by practically all with whom he associates. California banks not being safe, he hides his gold, only to have some of it apparently fall into the hands of his murderer.

If John Marsh was accused of not being an M. D., he apparently used such medical knowledge as he possessed to the advantage of his fellow men. His library consisted of his Bibles (English, French and Spanish), the "Odes of Anacreon," the inevitable Paine's "Works in Verse and Prose," and Johnson's "Lives of the English Poets," a medical book which he had bought from one of the Boston shops, a book on horticulture, and several written in Greek and Spanish. His medical armamentarium we know little about. Possibly his most noteworthy remedy was quinine, which he administered as early as 1836 in California. It should be remembered that this alkaloid was discovered in 1820 by Pelletier and Caventou. Hence its use on the westernmost frontier within two decades is truly remarkable. In California he received a set of surgical instruments from a Missouri emigrant who passed through his ranch in 1841. In spite of his meager medical training, John Marsh is re-

ferred to as the first American "physician" in California. His California wife, a former school teacher, apparently practiced on their Indians during his absence. The alcalde of San Jose, sending for help, also sent word that "according to the books the symptoms which one may recognize seem to be either of dropsy or anasarca," thus showing that the early immigrants occasionally provided themselves with presumably popular medical treatises.

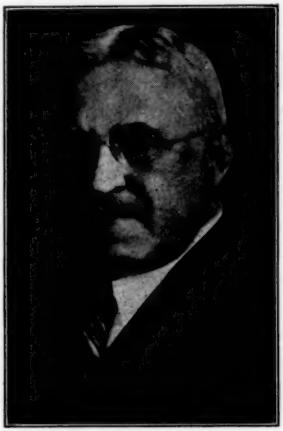
If in the early days of Massachusetts Colony, Giles Firmin complained to Governor Winthrop that he could not make a livelihood in Massachusetts as medical practitioner, and was "strongly set upon to study divinitie," it will be readily understood that John Marsh could not make a livelihood by practicing medicine in California during the thirties of the eighteenth century, even if he demanded fifty heads of cattle or a larger number of hides in payment for a visit. As already pointed out, he apparently wanted to make up for his disappointment, so far as his medical studies were concerned, by accumulating a fortune. This he did, not only by becoming a successful gold miner, but even before by the purchase of a large ranch in San Joaquin valley. Though murdered when only fifty-six years of age, he left an enormous estate with the finest homestead in California to the son of his French-Indian mate and the daughter of his schoolmam wife, an estate which is now "dotted with villages, factory towns and peaceful farms. It is the heart of the most productive area of San Joaquin Valley. Steamboats plow its waterways. A railroad traverses its extent." It is referred to as "the first center of American civilization in California."

While we feel that the Quaker Forty-niner failed as a business man, but remained true to his manhood, one cannot help but feel that the life story of John Marsh is about the most pitiable biography one cares to read and this in spite of the gold hoarded by him and his success in bringing California into the United States.

HENRY KENDALL MULFORD

Fifty Years of Service in the Making of Dependable Medicines

ACCLAIMED as one of the men who have accomplished much in the promotion of public health and the saving of human lives, as a result of work in biological science, Dr. H. K. Mulford was honored with a dinner in celebration of his golden pharmaceutical anniversary at the Union League, Philadelphia, on the evening of October 31st, 1935, by a group of distinguished scientists, physicians, chemists, pharmacists and educators. The event was sponsored by the National Drug Company, Mr. Charles E. Carr acting as chairman. Dr. Wilmer Krusen, president of the Philadelphia College of Pharmacy and Science, ably served as toastmaster. The story of the life of Dr. Mulford, as unfolded by men who have known him since his embarkation in the field of pharmacy, is of interest. Born in Bridgeton, N. J., October 10th, 1866, of old New England stock, H. K. (Henry Kendall) Mulford came from a family of old sea captains, and his forebears played an important part in local history. He attended the Bridgeton elementary school, later the South Jersey Institute, a military preparatory school with a curriculum comparable with present college work. Starting his drug career at the age of eighteen in the employ of Dodge & Olcutt, New York (the oldest essential oil house in this country), appreciating at this early period the need for a sound basis on which to begin his life's work, he returned to Philadelphia. He secured a job (not a position) in the drug store at Eighteenth and Market Streets, Philadelphia, operated by the later world-wide known teachers, Dr. Joseph P. Remington and Dr. L. E. Sayre. Everyone in pharmacy knows the high influence in American pharmacy of Remington and Sayre, and this first employment in a retail drug store furnished a fitting background for the future that Dr. Mulford has made for himself.



Henry Kendall Mulford

When Professor Remington decided to devote his full time to the Philadelphia College of Pharmacy and the U. S. P. work, he disposed of his interest in the retail store to Dr. Sayre. Within a few months Dr. Sayre was elected as Dean of the College of Pharmacy of the University of Kansas and he sold one-half interest to Dr. Mulford, who, having previously qualified as proprietor by passing the State Board, was in charge of the business. In the interim, Dr. Mulford took the pharmacy course at the Philadelphia College of Pharmacy and after waiting a year, because of age requirements, at the age of twenty-one he became a full fledged pharmacist, and the complete owner of this drug store. In the pharmacy (now nearly 160 years old) in which Dr. Mulford started his actual pharmaceutical experience, Henry Bowers made glycerine; Samuel Eastbrook perfected medicated lozenges; Drs. Remington and Sayre developed their background and Dr. Mulford started his work on the standardizing of drugs and later began his research in the biological field. He was the first in this country to supply diphtheria antitoxin for use by the medical profession distributed through the pharmacist.

Besides making his own U. S. P. and N. F. preparations, being of an originative type, Dr. Mulford began perfecting and manufacturing various pharmaceutical specialties, and in 1890 he formed the firm bearing his name, the H. K. Mulford Company, and manufactured for distribution through the wholesale and retail drug trade a line of pharmaceuticals featuring compressed tablets, for the manufacture of which he perfected and patented the well known Crown Tablet Machine.

Associated with Dr. Mulford at the outset of this company was Dr. E. V. Pechin, a graduate of the Philadelphia College of Pharmacy, and now retired.

In 1893, Dr. Mulford began studies on the production of diphtheria antitoxin, and associated with him leaders in bio-chemical research work. Included were such scientists as Dr. Joseph McFarland, now professor of pathology, University of Pennsylvania; Dr. Leonard Pearson, Dean of Veterinary School of Medicine, University of Pennsylvania; Dr. D. H. Bergey, former professor of bacteriology and director of hygiene of the University of Pennsylvania Medical School; Dr. A. P. Hitchens, now Major M. C. U. S. Army; Dr. C. P. Brown, clinical pathologist, United States Veterans

Hospital; Dr. Chas. E. Van der Kleed; A. Homer Smith, Chas. E. Gery, J. L. Tiffany, George R. Wilkes (now sales manager of the National Drug Company), Geo. Galbraith, H. Chandler Smith, Dr. Robert R. Fischelis and many others.

The progress in biological history during the period from 1893 to 1919 of the company bearing his name is emblematical of the foresight of Dr. Mulford. Success was largely due to his dynamic energy combined with his dominant characteristics of ethics in pharmaceutical manufacturing, perseverance, and his love of fellowman, which not only influenced the selection of his associates but secured active co-operation of his co-workers—for he believes in giving authority with responsibility.

Realizing the principle that life itself is the application of the colloidal equation, in 1921 Dr. Mulford directed his work to colloid chemistry and later established the Mulford Colloid Laboratories. His work in this field has been successful in the production of medicinal colloids (sulphur, manganese, iron and iodine, etc.), and in developing antigens for the treatment of poison ivy.

In 1926 he was given the directorship of the Research and Biological Laboratories of the National Drug Company of Philadelphia. With sound judgment he selected Dr. C. P. Brown as medical director for the National Drug Company, thus renewing an association that started more than twenty-seven years previously. In these research laboratories at 5109 Germantown Avenue, Philadelphia, and at their biological laboratories at Swiftwater, Pa., Dr. Mulford actively works (he calls it play) in developing biological products for the interests of humanity, and in striving to protect and save human lives.

Ethical to the highest degree, Dr. Mulford believes in the highest standards of manufacture of biological products, and in their distribution through the ethical pharmacist by selective distribution. In addition to having established the first biological laboratory in the United States, for the production of diphtheria antitoxin, Dr. Mulford was one of the first advocates of the development of the standardization of biologicals and galenicals. In this latter work, he was assisted by Dr. Edgar Fahs Smith, Dean of the University of Pennsylvania, Dr. George H. Meeker, now Dean of the Post Graduate School of Medicine of the University of Pennsylvania, the late Dr. A. C. Abbott, professor of bacteriology and director of

hygiene, University of Pennsylvania Medical School, and his assistant, Dr. David H. Bergey, who succeeded Dr. Abbott as professor and director. Dr. Bergey was the first scientist in this country to check test antitoxins for potency according to the Ehrlich standards and Dr. Mulford's diphtheria antitoxin was the first that he so tested and it is significant that after a forty-year friendship, Dr. Bergey is now a co-worker with Dr. Mulford and is the director of research and bacteriology for the National Drug Company.

The degree of master of science was conferred upon Dr. Mulford in 1918, and the highest honor in pharmacy, master in pharmacy, was conferred upon him by his Alma Mater, the Philadelphia College of Pharmacy and Science, in 1933. He is a member of the American Pharmaceutical Association, American Drug Manufacturers Association, American Pharmaceutical Manufacturers Association, American Chemical Society, The Franklin Institute and the Union League Club. This journal joins in hearty congratulations in this, his golden jubilee of service to humanity, and wishes him many more years of healthful, happy and prosperous service in his chosen professions, pharmacy, chemistry, biology.

SUNBURN LOTIONS—The literature of sunburn treatment is both profound and prolific, and there is available a vast array of sunburn preventives and palliatives, not all of which are as practically propitiating as they are theoretically intriguing. Inland formula compilers, and arm-chair depositors of graphite on cellulose, have juggled long with angstrom units, actinic rays, selective filters, absorption spectra and other scientific doo-dads, and they have out of the wealth of their wisdom offered to the sun-bitten trade some queer combinations of chemicals scientifically approved and selected.

Yet when the writer of this note, forgetting that his Nordic ancestry gave him a tissue-thin skin during a piscatorial excursion unduly exposed his person to a blistering clystering sun, he paid the full penalty of his heresy, by a vicious, external attack of sunitis.

And it was not the new-fangled synthetics, nor the widely heralded commercial concoctions that eased his fiery pains but an old-fashioned formula found and filled by an old-fashioned apothecary who lives by the side of the sea where the sun shines brightest. Here it is—a gun-shot prescription for a sun-shot predicament:

Milk of magnesia.
Calamine lotion, N. F. V.
Alkaline aromatic solution, N. F. V. of each . . . 4 fl. oz.
Spirit of camphor . . . . . 1 fl. oz.
Paregoric . . . . . 2 fl. oz.
Alcohol to make . . . . . 16 fl. oz.
Mix, and apply locally.

The same seashore apothecary generously offered the formula which he found a fine preventive, and which from one fisherman to another, is hereby heartily commended:

Acetanilid . . . . . 1 dr.
Camphor . . . . . 1 dr.
Menthol . . . . . 10 grams
Phenol . . . . . 1 dr.
White lard oil . . . . . 4 fl. oz.
Olive oil . . . . . 4 fl. oz.

Allow the solids to fuse together in a mortar. Incorporate this eutectic mixture with the oil.

Color to a pleasing brownish tan with an oil soluble brown which can be secured from any dyestuff merchant.

SCIENTIFIC AND TECHNICAL ABSTRACTS

Compiled by Linwood F. Tice, M. Sc.

The Relationship of Drug Therapy to Agranulocytosis. R. R. Kracke and F. P. Parker. *J. Am. Med. Assoc. 105,* 960 (1935). This article presents a very comprehensive picture of the clinical evidence supporting the theory that certain drugs, namely, amidopyrine, dinitrophenol and possibly other closely related drugs provide the most important etiologic factor in agranulocytosis.

This disease is known to have produced 1500 deaths in this country alone in a three-year period ending in 1934.

The clinical picture presented by this disease is a marked diminution or total absence of granulocytes of the peripheral blood followed by loss in cellular resistance with various infectious processes resulting.

The list of forty-six American proprietaries containing amidopyrine is included and the recommendation made that drugs containing this substance as an ingredient be discouraged for widespread use and prescribed by physicians only in non-refillable prescriptions.

Volumetric determination of Iodide Ions by the Method of Tajans. E. J. Kocsis, *Z. Anorg. Allgem. Chem. 221,* 318 (1935) through *C. A. 29,* 2476 (1935). Two dyes "Diaminechtbordeaux 6 B. S." and "Diaminechtviolet B. B. N." sold by Cassella & Co. are suitable for use in the titration of iodides with silver nitrate. When the equivalence point is reached the dyes are strongly adsorbed by the silver iodide precipitate and the color changes to a yellow green. Chlorides and bromides may not be titrated with these indicators with satisfactory results. The second dye can be used in acetic acid solution and iodides may then be determined in the presence of chlorides.

A Note on the Analysis of Oil of Peppermint. G. Baumgarten *Dtsch. Apoth.-Ztg. 50,* 364 (1935) through *Pharm. Zentral. 76,* 586

(1935) No. 38. In the determination of menthol in oil of peppermint by acetylization and subsequent saponification of the acetylization product, a dark color is sometimes produced which makes the use of phenolphthalein as an indicator somewhat difficult. The author recommends an addition of methylene blue to the phenolphthalein. This produces instead of a change from red to yellow or brown at the endpoint a change from reddish-violet to green or olive-green.

After acetylization and saponification there is added 1 cc. of a phenolphthalein solution, 1.5-2 cc. of a solution of methylene blue T. S. diluted 1-10 and then the mixture is titrated with 0.5 N. HCl until a color change from reddish-violet to green is produced.

A Reaction for Distinguishing Quinine form Quinidine. L. Rossi and J. A. Sozzi *Quim e ind. 11,* 199-201 (1934) through *C. A. 29,* 2305 (1935) No. 7. Inasmuch as quinine and quinidine are optical isomers most of their reactions are identical. Thirty commonly used alkaloidal reagents give the same test with both. The differentiating test is as follows: To a solution of the pure alkaloid in very dilute sulfuric acid add a drop of $KI.I_2$ solution shake and dilute, if the precipitate is heavy, until a light translucent suspension is obtained. In the case of quinine the precipitate appears dark brown while if the sample is quinidine it will appear yellow.

Retarding Rancidity. W. L. Morgan, *J. Ind. Eng. Chem. 27,* 1287 (1935) No. 11. The protection of various substances against the accelerating effect of light in the production of rancidity has become of considerable importance in the packaging industry. Although light is not the only factor concerned with the development of oxidative rancidity, it is frequently the predominating influence.

Various recommendations have been made concerning the type of wrapping offering adequate protection for products subject to rancidity development. Some of these are misleading and not in accordance with the findings of later work.

A large number of specially prepared cellulose films of a wide variety and shade of colors were used in determining which rays in sunlight are the accelerators of rancidity. The development of rancidity was determined both organoleptically by taste and by the Kreis test.

As a result of this study it was found that the visible rays of green, yellow and red greater than 4900 Å have relatively little effect in producing rancidity whereas blue and ultraviolet light is very effective in the production of rancidity. A special yellow, rancidity retarding, transparent, cellulose sheeting known as "Sylphrap R. R. Old Gold" has been developed which is opaque to ultraviolet and blue light. This wrapping material should provide an excellent covering for packages of foods and drugs subject to oxidative change accelerated by light.

The Detection of Certain Bases of Alkaloidal Nature by an Extremely Sensitive Reaction. H. Wachsmuth, *J. pharm. Belg. 17,* 795 (1935) No. 40 through *Squibb Abstract Bulletin 8,* No. 45 (1935). A new procedure for the detection of certain bases of alkaloidal nature is as follows: To 10 cc. of a very dilute solution of the base add 0.5 cc. of a 0.15 per cent. solution of $CuSO_4$ and then 1-2 drops of a 1 per cent. solution of KCN. The solution becomes colored immediately and the reaction occurs in the cold. The reaction is extremely sensitive but too great a concentration of base must be avoided or clouding and precipitation may result. Excess cyanide is objectionable and hastens fading. This reaction is produced not only by cyanide but also with thiocyanate, ferricyanide and by nitroprusside in the presence of copper.

Morphine gives a greenish-yellow color (sensitivity 1/20,000); amidopyrine a violet (sensitivity 1/700,000); apomorphine red changing to pink, brown, gray and finally green (sensitivity 1/1,200,000); and adrenalin a red color (sensitivity 1/5,500,000).

In the case of apomorphine the final green color may be extracted by various organic solvents such as amyl alcohol, chloroform, methyl benzoate, etc. giving blue or violet-blue colors.

The Treatment of Arthritis With Colloidal Sulfur. S. C. Woldenberg *Southern Med. J. 28,* 875 (1935) No. 10, through *Squibb Abstract Bulletin 8,* 1564 (1935), No. 44. The author reports results of the treatment of 250 cases of arthritis in which the procedure of removal of foci of infection, control of diet, physiotherapy and corrective orthopedics was followed by the administration of colloidal sulfur, in aqueous suspension for intravenous administration, and in olive oil for intramuscular use. Every case showed clinical improvement in a relatively short time with no recurrence of symptoms. Furthermore, no joint changes were observed. The recommendation is made by the author that colloidal sulfur therapy be used early to prevent both unnecessary suffering and contractural deformities.

The Emulsifying Ingredient in Egg Yolk. H. M. Sell, A. G. Olsen, R. E. Kremers, *J. Ind. Eng. Chem. 27,* 1222 (1935) No. 10. Due to the well known fact that lecithin is contained in egg yolk, the emulsifying properties of egg yolk in preparing mayonnaise has been ascribed to its lecithin content.

Inasmuch as an addition of lecithin to egg yolk did not improve its emulsifying properties, experiments were conducted in which egg yolk was separated into its various components and then each of these subjected to an examination as to its emulsifying action.

The results indicate that a substance lecitho-protein is responsible for the greatest stabilizing influence of all the constituents present. This material is present to the extent of about 32.5 per cent. in the raw yolk.

Two other components of egg yolk, cephalin and lecithin were found to quite definitely detract from the consistency of a mayonnoise made by their addition to the egg yolk prior to emulsification.

A New Method for the Determination of Water. E. v. Migray, *J. Ind. Eng. Chem. Anal. Ed. 7,* 348 (1935). This method is an extension of the xylene distillation method and has the advantage that small quantities of water can be determined accurately even when the material contains only a few tenths per cent. of water.

The procedure is briefly as follows: The material is distilled with xylene or toluene and the distillate dehydrated with a weighed quantity of anhydrous copper sulfate. The copper sulfate is then filtered out in a tube filter, washed with ether, dried in an evacuated desiccator and weighed. The increase in weight represents the water present.

Yeast—In Medicine

In medicine value, yeast was early recognized. In Eber's Papyrus, a medical treatise, written approximately 1500 B. C., a reference is made to the therapeutic use of yeast. Already at that time yeast was recommended as an ingredient in a prescription for constipation. Hippocrates and Pliny the elder used yeast as a curative agent.

Oldest is probably the use of yeast as an agency to leaven dough in breadmaking or to cause fermentation. A reference in the Bible is of interest (Exodus 13:17): "Unleavened bread shall be eaten seven days; and there shall be no leavened bread seen with thee, neither shall there be leaven seen with thee in all thy quarters."

The first record of the microscopic description of yeast is furnished about 1660 by Leeuwenhoek, the obscure Dutch pioneer and student of micro-life, who described yeast as small, round, or ovoid particles. The first chemical record, evidently, was provided by Cavendish, who observed the formation of carbondioxide gas during fermentation, of hydrogen gas during putrefaction. Lavoisier, as the first, formulated the process of alcoholic fermentation as follows: $C_6H_{12}O_6 = 2C_2H_5OH + 2CO_2$ (+ 27 Calories) which reaction, with the exception of certain minor reactions, is recognized as correct today. The sugar, according to Lavoisier, is split into two parts; one is oxidized at the expense of the other. Thus an oxidized and a reduced substance are formed, the fermentation process essentially is an oxydo reaction, the oxygen of the atmosphere having no part in the process. Thenard (1803) also added to the progress of knowledge when he noted that the deposits occurring in fermented liquids resembled brewer's yeast. Then Exleben (1818), Latour (1835), Schwann (1837), Kuetzing (1837), possibly independently, observed yeast as a living organism and concluded that alcoholic fermentation depended upon the presence of living cells.

Berzelius attributed the fermentative activity of yeast to a catalytic force, and Liebig as well as Woehler, the foremost chemists of their time (1839) supported the physico-chemical explanation and bitterly opposed the biological theory that fermentation was due to a living form. In the highly scientific "Woehler and Liebig's Annalen" in 1839 appeared an anonymous article ridiculing the notion of yeast as a creature which eats sugar and excretes carbon dioxide and alcohol: "I am in the act of unraveling a new theory of vinous fermentation. I came upon the trail of this, until now so mysterious a change, in the simplest manner in the world and regard it as fully settled. This discovery too shows again how simple are the means of which nature makes use, to bring forth the most wonderful phenomenon; I owe thanks to the use of a remarkable microscope."—(*Pop. Sc.* Vol. X, p. 110.)

Arsenic in Natural Waters

Thus the renowned spring at Vichy, France, provides a mineral water which, among other constituents, contains a little arsenic, namely, about two parts per million. The Koch Brunnen in Wiesbaden, the springs at Orsola in the Tyrolean Alps, the Lorenz Quelle in Switzerland, and the waters of numerous other springs in Europe, contain arsenic. So likewise do some of our American spring waters, particularly those of the Yellowstone region—even Old Faithful, the geyser renowned because of its reliability of performance, and which no visitor to the Yellowstone misses seeing, spouts a little arsenic.

With reference to arsenical mineral waters, it may be said that, although they have been imbibed by countless thousands, no injurious results attributable to the small dosages of arsenic have been noted. Apparently, the poison, in quantities so exceedingly small, is not injurious at all. This is a reassuring and a comforting fact, for it is difficult to keep minute traces of arsenic out of our diet.

As is well known, the waters of the ocean, embodying the leachings of the uppermost strata of the earth's crust, carry countless tons of compounds of arsenic, the content varying from one to eight parts per ten million. And since it is a well-known fact that marine organisms may exhibit the property of selective absorption and assimilation of certain sea-water constituents, with the result that they ac-

cumulate in their own tissue higher percentages of such substances than those observed in the fluid in which they live, we need not be surprised to find our sea food more highly arseniferous than ocean water itself. Such is really the fact in respect to crabs, lobsters, clams, oysters, and our edible salt-water fish. Every time we eat cod, for example, or herring, we ingest a small dose of arsenic; and when we take cod-liver oil, we get a slightly larger dose, in proportion, for in fish the arsenic seems to be localized mainly in the fat. There is, however, no danger from arsenic in sea food or its products. One could eat seven or eight pounds of baked cod, or drink an entire pint of cod-liver oil, without incurring danger as far as the arsenic is concerned, for the quantity of the latter involved in such immoderate food portions would not exceed that of a safe medicinal dose of the poisonous substance.—(*Pop. Science,* Vol. X, p. 96.)